

Outcome of Debridement and Retention in Prosthetic Joint Infections by Methicillin-Resistant Staphylococci, with Special Reference to Rifampin and Fusidic Acid Combination Therapy

T. N. Peel,^{a,b} K. L. Buising,^a M. M. Dowsey,^{b,c} C. A. Aboltins,^a J. R. Daffy,^a P. A. Stanley,^a P. F. M. Choong^{b,c}

Department of Infectious Diseases, St. Vincent's Hospital, Melbourne, Victoria, Australia^a; Department of Surgery, University of Melbourne, Melbourne, Victoria, Australia^b; Department of Orthopaedic Surgery, St. Vincent's Hospital, Melbourne, Victoria, Australia^c

The management of prosthetic joint infections remains a clinical challenge, particularly infections due to methicillin-resistant staphylococci. Previously, this infection was considered a contraindication to debridement and retention strategies. This retrospective cohort study examined the treatment and outcomes of patients with arthroplasty infection by methicillin-resistant staphylococci managed by debridement and retention in conjunction with rifampin-fusidic acid combination therapy. Over an 11-year period, there were 43 patients with infection by methicillin-resistant staphylococci managed with debridement and retention. This consisted of close-interval repeated arthrotomies with pulsatile lavage. Rifampin was combined with fusidic acid for the majority of patients (88%). Patients were monitored for a median of 33.5 months (interquartile range, 20 to 54 months). Overall, 9 patients experienced treatment failure, with 12- and 24-month estimates of infection-free survival of 86% (95% confidence interval [CI], 71 to 93%) and 77% (95% CI, 60 to 87%), respectively. The following factors were associated with treatment failure: methicillin-resistant *Staphylococcus aureus* (MRSA) arthroplasty infection, a single surgical debridement or ≥ 4 debridements, and the receipt of less than 90 days of antibiotic therapy. Patients with infection by methicillin-resistant coagulase-negative staphylococci (MR-CNS) were less likely to fail treatment. The overall treatment success rate reported in this study is comparable to those of other treatment modalities for prosthetic joint infections by methicillin-resistant staphylococci. Therefore, the debridement and retention of the prosthesis and rifampin-based antibiotic therapy are a valid treatment option for carefully selected patients.

Methicillin-resistant (MR) staphylococci are common and challenging pathogens associated with prosthetic joint infection (PJI) (1). Worse treatment outcomes have been reported for PJI by MR *Staphylococcus aureus* (MRSA) than for other pathogens, particularly with the debridement and retention (DAR) of the prosthesis (2–8). Treatment algorithms recommend against DAR for patients with MRSA (1). In addition, there have been few studies describing the outcomes of PJI caused by MR coagulase-negative staphylococci (MR-CNS).

MATERIALS AND METHODS

Study design. The aims of this retrospective cohort study were to describe the management approach and outcomes of DAR in patients with arthroplasty infection by MR staphylococci and to identify factors associated with treatment failure. All patients were monitored from the date of diagnosis of infection until discharge from the clinic or death. The study design was reviewed and approved by the Hospital Ethics Committee (approval number QA040-08).

Study population. The study was conducted at St. Vincent's Hospital Melbourne (SVHM), a university-affiliated, tertiary hospital. The study population comprised all patients who had knee or hip arthroplasty performed over the period of January 2000 to December 2010. Patients were included in the study if MR staphylococci were isolated from two or more intraoperative specimens, including patients with polymicrobial infections. Cases were identified from a review of the SVHM arthroplasty registry and microbiology database (9). The SVHM arthroplasty database contains information on 5,603 prosthetic hip and knee replacements performed over the study duration. A minimum of 12 months of follow-up data was recorded for 98% of the patients in this database. Data were extracted from a review of the medical chart. Some included patients were included in data from previous reports (10, 11).

At SVHM, patients with PJI are managed according to an established

protocol described previously (9). In short, patients with early and hemo-genous PJI with stable implants are managed by DAR, entailing prompt arthrotomy and aggressive debridement (1, 12). Patients typically undergo 3 arthrotomies and debridement within a 7- to 10-day period. Mobile parts are not routinely exchanged, but the liner is changed where feasible. Patients receive a short course of intravenous antibiotics before commencing oral antibiotics with activity against biofilm-associated bacteria. At SVHM, the majority of patients receive rifampin in combination with fusidic acid for staphylococcal infections and ciprofloxacin for Gram-negative infections.

Microbiology. All intraoperative specimens were cultured on blood agar and chocolate agar incubated in 35°C CO₂ and prereduced anaerobic agar at 35°C anaerobically for 48 h. In addition, tissue specimens were incubated in thioglycolate broth for 7 days in 35°C O₂. Specimens from the thioglycolate broth were subcultured onto blood agar and incubated aerobically and anaerobically if the broth became cloudy. Terminal cultures were not performed on broth specimens.

Sensitivity testing on all staphylococcal isolates was performed with a Vitek-2 system (bioMérieux, Durham, NC), using current Clinical and Laboratory Standards Institute breakpoints.

Definitions. All microbiology cultures results were considered significant if the same microorganism(s) was isolated from two or more intraoperative specimens.

Based on recent literature, treatment failure was defined as either

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Address correspondence to T. N. Peel, tpeel@student.unimelb.edu.au.

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TABLE 1 Demographics and clinical, microbiological, and biochemical features at presentation with PJI by MR staphylococci

Variable	Value for patients (n = 43)
Median age (yr) (IQR)	73 (67–77)
No. (%) of female patients	23 (53)
No. (%) of patients with index arthroplasty site of:	
Hip	28 (65)
Knee	15 (35)
No. (%) of patients with indication for index arthroplasty	
Primary joint replacement	35 (81)
Revision arthroplasty for mechanical loosening	6 (14)
Revision arthroplasty in patient with history of infection	2 (5)
Median body mass index (kg/m ²) (IQR)	32 (28–39)
No. (%) of patients with diabetes mellitus	9 (21)
No. (%) of patients with rheumatoid arthritis	3 (7)
Implant age at date of presentation with infection (days) (IQR)	16 (12–21)
Duration of symptoms of prosthetic joint infection (days) (IQR)	6 (2–14)
No. (%) of patients with symptom at presentation with prosthetic joint infection	
Fever ($\geq 37.5^{\circ}\text{C}$)	15 (35)
Purulent discharge from surgical wound	30 (70)
Pain involving the index prosthetic joint	16 (37)
Sinus tract overlying index prosthetic joint	2 (5)
Hypotension (systolic blood pressure of ≤ 90 mm Hg)	2 (5)
Median white cell count (10^9 cells/liter) (IQR)	8.2 (6.2–9.1)
Median C-reactive protein level (mg/liter) (IQR)	46 (16–116)
Median erythrocyte sedimentation rate (mm/h) (IQR)	55 (41–70)
No. (%) of patients with blood culture result	
No blood cultures obtained	27 (63)
Negative	13 (30)
Positive	3 (7)

death from PJI or one or more of the following at a time subsequent to the original presentation with PJI: (i) a reoccurrence of PJI due to the same microorganism, (ii) an occurrence of PJI due to a different microorganism, (iii) the development of a sinus tract, or (iv) the presence of purulence surrounding the prosthesis observed intraoperatively (13).

Microbiological recurrence was considered if patients experienced treatment failure with the isolation of the same microorganism at a time subsequent to the original presentation.

Statistical analysis. Descriptive statistics were used to summarize and report the data. Descriptive analyses were based on percentages and frequencies for categorical variables and for continuous variables, means and standard deviations (SD), medians and interquartile ranges (IQR), or ranges if the data were skewed. The Kaplan-Meier survival method was used to estimate 12- and 24-month survival rates free from treatment

TABLE 2 Microbiology results from intraoperative specimens

Infection type and organism(s)	No. (%) of patients (n = 43)
MRSA infections	
MRSA monomicrobial infection	16 (37)
MRSA plus <i>Enterococcus faecalis</i>	4 (10)
MRSA plus <i>Escherichia coli</i>	2 (5)
MRSA plus <i>Morganella morganii</i> + <i>Proteus mirabilis</i>	1 (2)
MRSA plus methicillin-sensitive <i>Staphylococcus epidermidis</i>	1 (2)
MR-CNS	
MR-CNS monomicrobial infection	11 (26)
MR-CNS infection involving 2 different MR-CNS species	2 (5)
MR-CNS plus <i>Enterococcus faecalis</i>	2 (5)
MR-CNS plus <i>Serratia marcescens</i>	1 (2)
MR-CNS plus <i>Escherichia coli</i>	1 (2)
MR-CNS plus <i>Proteus mirabilis</i>	2 (5)

failure. Logistic regression was performed to identify risk factors associated with treatment failure upon a univariate analysis. All reported *P* values were two tailed, and for each analysis, a *P* value of <0.05 was considered statistically significant. All analyses were performed by using Stata 11.2 (StataCorp, College Station, TX).

RESULTS

Over the study period, there were 108 PJI (62 prosthetic hip and 46 prosthetic knee infections), of which 47 infections were due to MR staphylococci (44%). Four patients underwent resection of the prosthesis and were excluded from the analysis. Therefore, 43 patients were included in the study. All patients presented with early PJI (presenting within 3 months of implantation), except for 2 patients, with PJI presenting between 3 and 24 months from implantation. There were no late infections. The median implant age was 16.5 days (IQR, 11 to 22 days). In keeping with early presentations, the majority of patients (95%) presented with complications involving the surgical wound. The demographic characteristics and presenting features of the cases are included in Table 1. The majority of infections (63%) were monomicrobial. Polymicrobial infections typically involved MR staphylococci plus enteric flora (Table 2).

Surgical management. All patients were managed by DAR consisting of arthrotomy and thorough synovectomy with the removal of all inflamed tissue, clot, and fibrinous tissue, followed by normal saline pulsatile lavage of the joint and instillation of alcoholic chlorhexidine, povidone-iodine, and hydrogen peroxide. Patients underwent multiple debridements, in keeping with established protocols, and after each operation, primary closure in layers was employed, and suction drains were left *in situ*. The liner was changed in 42% of patients, and mobile parts were not changed. Patients had a short duration of symptoms until debridement (median, 7 days; IQR, 5 to 15 days). The majority of patients underwent surgery within 24 h of admission (median, 1 day; IQR, 0 to 3 days) and underwent three arthrotomies (70%); the median number of debridements was 3 (range, 1 to 9).

Medical management. All patients except one initially received parenteral vancomycin alone or in combination. The patient who did not receive parenteral vancomycin was commenced on rifampin and fusidic acid immediately after the verification of

culture results. The median duration of vancomycin treatment was 12 days (IQR, 7 to 22 days). Patients with polymicrobial infections received a longer course of parenteral antibiotics (median, 29 days; IQR, 13 to 45 days). All patients with infections involving Gram-negative bacilli received a beta-lactam antibiotic in addition to vancomycin. Three patients experienced adverse effects from parenteral antibiotic therapy: one patient developed a rash, and two patients developed acute renal failure. Antibiotic therapy was ceased for 2 patients due to the severity of the reaction (1 patient with rash and 1 patient with acute renal failure).

Rifampin combination therapy was the mainstay of oral antibiotic therapy for 93% of the patients. Of the three patients who did not receive rifampin combination therapy, two patients had *Staphylococcus epidermidis* isolates that were resistant to rifampin and were therefore treated with pristinamycin plus ciprofloxacin for one patient and with clindamycin plus amoxicillin for the other. A third patient with significant comorbidities requiring multiple medications, including warfarin, was treated with pristinamycin to avoid a rifampin-warfarin interaction. No patient in this group subsequently failed treatment. For the remainder of the patients, rifampin was combined with fusidic acid for 88%, with ciprofloxacin for 5%, and with pristinamycin for 8% of the patients. The doses of oral antibiotics were as follows: rifampin at 300 mg twice daily, fusidic acid at 500 mg three times daily, ciprofloxacin at 500 to 750 mg twice daily, and pristinamycin at 1,000 mg three times daily. The doses were maintained throughout the course of treatment with no dose reduction. Rifampin was commenced within 16 days of presentation for 75% of patients.

Five patients (12%) experienced adverse reactions to the oral antibiotic combinations, including gastrointestinal upset (two patients), acute renal failure (one patient), and derangement of liver function tests (one patient), and one patient receiving ciprofloxacin developed Achilles tendinopathy. The adverse reaction was severe enough to necessitate the cessation of the antibiotic for 4 patients (10%): 1 patient with deranged liver function tests, 1 patient with Achilles tendinopathy, 1 patient with acute renal failure, and 1 patient with severe nausea and vomiting. Subsequently, one patient requiring a cessation of antibiotic therapy failed the treatment of PJI. Patients received a median duration of 341 days (IQR, 199 to 398 days) of oral antibiotic therapy.

Patient outcomes. Patients were monitored for a median of 33.5 months (interquartile range, 20 to 54 months) after the date of presentation with PJI. Four patients (9%) had died from causes unrelated to PJI; there were no deaths directly attributable to PJI. Patients were monitored after the cessation of antibiotic therapy for a median of 24 months (IQR, 5 to 42 months). Nine patients experienced treatment failure according to the *a priori* definition. Eight of these patients had PJI by MRSA. The median time to treatment failure was 5 months (IQR, 3 to 13 months). Two patients failed treatment more than 6 months from presentation with PJI, failing at 6 and 17 months, respectively. Eight patients were still receiving antibiotic therapy at the time of failure; only one patient had ceased oral antibiotics at the time of failure. Four patients had microbiological failure (9%); three of these patients had cultured organisms with resistance to rifampin and fusidic acid. Poor adherence to antibiotic therapy was documented for two of these patients. One other patient with MRSA infection subsequently had *Staphylococcus epidermidis* resistant to rifampin and fusidic acid isolated. The subsequent approach for patients with treatment failure is outlined in Table 3. Of note, 5 patients

TABLE 3 Patients with treatment failure and subsequent management

Patient	Organism(s) isolated	Initial medical management ^a				Receiving antibiotic therapy at time of failure ^b	Criterion for treatment failure ^b	Microbiological failure	Rifampin resistance detected	Management of treatment failure	Outcome of retreatment	Time of follow-up after treatment failure (mo)
		Parenteral antibiotic(s)	Duration of parenteral antibiotic(s) (days)	Oral antibiotic(s)	Duration of oral antibiotic(s) (mo)							
1	MRSA plus <i>Escherichia coli</i>	V, CTX	52	R, FA	17	Yes	3	No	No	Above-knee amputation	Free from subsequent failure	19
2	MR-CNS (2 different isolates)	V	7	R, FA	1	Yes	1	Yes	Yes	Two-stage exchange	Free from subsequent failure	42
3	MRSA plus <i>Escherichia coli</i>	V, M	59	R, FA, C	7	Yes	1	Yes	No	Life-long suppression with rifampin and fusidic acid ^c	Life-long antibiotic suppression	30
4	MRSA	V	7	R, FA	6	Yes	2	No	Yes ^d	Further debridement followed by clindamycin and amoxicillin for 24 mo	Developed sinus tract	24
5	MRSA	V	14	R, FA	1	Yes	4	No	No	Debridement and rifampin and fusidic acid for 22 mo	Free from subsequent failure	24
6	MRSA	V	2	R, FA	4	Yes	1	Yes	Yes	Two-stage exchange	Free from subsequent failure	68
7	MRSA	V	12	R, FA	1	Yes	2	No	No	Debridement and 6 mo ciprofloxacin	Free from subsequent failure	74
8	MRSA	V	15	R, FA	1	Yes	1	Yes	Yes	Resection arthroplasty	Free from subsequent failure	4
9	MRSA plus <i>Enterococcus faecalis</i>	V	3	R	2 ^e	No	4	No	No	Recommended rifampin and fusidic acid for 15 mo	Free from subsequent failure	36

^a V, vancomycin; CTX, ceftriaxone; M, meropenem; R, rifampin; FA, fusidic acid; A, amoxicillin; C, ciprofloxacin.

^b Criteria for treatment failure were as follows: 1, recurrence of same microorganism(s); 2, isolation of a different microorganism(s); 3, periprosthetic purulence observed; 4, development of sinus tract.

^c The patient presented with a new diagnosis of myasthenia gravis requiring prolonged intensive care unit admission and was too unwell for further surgical interventions.

^d MRSE (methicillin-resistant *S. epidermidis*) resistant to rifampin and fusidic acid was subsequently isolated from the patient.

^e All oral antibiotics were ceased due to acute renal failure/acute interstitial nephritis.

TABLE 4 Univariate model of factors associated with treatment failure^a

Variable	Value for group		OR (95% CI)	P value
	Treatment success (n = 34)	Treatment failure (n = 9)		
Median age (yr) (IQR)	74 (69–77)	63 (59–77)	1.0 (0.9–1.0)	0.2
No. (%) of female patients	19 (83)	4 (17)	0.6 (0.1–2.8)	0.5
No. (%) of patients with knee arthroplasty	14 (93)	1 (7)	0.2 (0.02–1.6)	0.1
No. (%) of patients with index arthroplasty indication				
Primary	28 (80)	7 (20)	1 (ref)	
Aseptic revision	5 (83)	1 (17)	0.8 (0.08–8.0)	0.8
Septic revision	1 (50)	1 (50)	4 (0.2–72.2)	0.3
Median no. of days of symptoms (IQR)	7 (2–14)	4 (1–7)	1.0 (0.9–1.1)	0.3
No. (%) of patients with infection classification of:				
Early (≤ 90 days from implantation)	32 (78)	9 (22)	1 (ref)	
Delayed (> 90 days from implantation)	2 (100)	0		
No. (%) of patients with polymicrobial infection	12 (75)	4 (25)	1.5 (0.3–6.5)	0.6
No. (%) of patients with causative microorganism				
MRSA	16 (67)	8 (33)	9.0 (1.0–80.0)	0.049
MR-CNS	8 (89)	1 (11)	0.1 (0.01–0.9)	0.03
No. (%) of patients with no. of surgical debridements				
2–3	30 (91)	3 (9)	1 (ref)	
1	1 (25)	3 (75)	30.0 (2.3–386.3)	0.009
≥ 4	3 (50)	3 (50)	10.0 (1.4–73.3)	0.02
No. (%) of patients with liner changed	15 (83)	3 (17)	1.6 (0.3–7.4)	0.6
No. (%) of patients with microbiology cultures positive upon final debridement	20 (74)	7 (26)	2.5 (0.4–13.6)	0.3
Median no. of days of parenteral vancomycin treatment (IQR)	12 (9–17)	14 (7–23)	1.0 (0.9–1.1)	0.2
No. (%) of patients with duration of antibiotic therapy (oral and parenteral)				
> 365 days	18 (90)	2 (10)	1 (ref)	
180–365 days	13 (87)	2 (13)	1.4 (0.2–11.1)	0.8
90–180 days	2 (67)	1 (33)	4.5 (0.3–74.7)	0.3
< 90 days	1 (20)	4 (80)	36 (2.6–501.3)	0.008

^a OR, odds ratio; ref, reference. Boldface type indicates significant value ($P < 0.05$).

after retreatment still retained their original prosthesis. Of the remaining patients, 2 underwent two-stage exchange, 1 underwent resection arthroplasty, and 1 patient required an amputation to control the infection. Eight of the patients with treatment failure after subsequent retreatment remained free from a recurrence of infection after a median of 30 months of follow-up from the date of treatment failure (IQR, 21.5 to 55 months).

The 12- and 24-month estimates of infection-free survival were 86% (95% confidence interval [CI], 71 to 93%) and 77% (95% CI, 60 to 87%), respectively. The 12- and 24-month estimates of infection-free survival for MRSA were 79% (95% CI, 57 to 95%) and 65% (95% CI, 41 to 81%), respectively, and for MR-CNS, the estimate for infection-free survival was 95% (95% CI, 68 to 99%) for both 12 and 24 months. The following factors were associated with treatment failure: MRSA arthroplasty infection and single surgical debridement or ≥ 4 debridements. Patients with MR-CNS were less likely to fail treatment. The duration of antibiotic therapy was

challenging to assess as an independent factor for failure, given that the majority of patients were receiving antibiotic therapy at the time of treatment failure. While a duration of antibiotic treatment of < 90 days was associated with failure, no difference in the failure rate was observed with treatment durations of 90 to 180, 180 to 365, and > 365 days. Of note, microbiology cultures still detected the causative microorganism at final debridement for 63% of patients, but this did not impact management outcomes. In addition, changing of the liner was not associated with treatment failure (Table 4).

DISCUSSION

In the current study of 43 patients with PJI by MR staphylococci managed with debridement and retention of the prosthesis, we report a successful outcome for 34 patients (79%). In the cases of treatment failure, the same pathogen was reisolated from 4 patients at subsequent presentation. For 5/9 cases, it could be argued that the treatment failure may reflect superinfection with a second

organism or a failure to identify a second pathogen originally rather than a failure of the original antibiotic treatment directed at MR staphylococci. Furthermore, 91% of patients were able to retain their original prosthesis. The success rate reported in the current study is comparable to those reported previously for the two-stage exchange of the prosthesis for infections by MR staphylococci, which were variable, ranging from 50% to 79% (4, 5, 14–16). Importantly, the definition for treatment success reported in those studies varied from the maintenance of a functioning joint to the reisolation of the same infecting organism (2, 3, 14, 16).

Patients in this cohort had a short duration of symptoms prior to presentation to the hospital and underwent debridement within 24 h of presentation. The prompt recognition and management of the infection would impact the likelihood of treatment success (13, 17). Patients underwent multiple debridements, which differs from other centers, where single debridement is performed with the exchange of all mobile parts, including liners (12). Indeed, in the current study, patients undergoing a single surgical debridement had a 30-fold-increased risk of treatment failure. In contrast, in a large Spanish multicenter study of *Staphylococcus aureus* infections managed with DAR, 88% of patients underwent a single debridement, and the need for ≥ 2 debridements predicted treatment failure, as did not exchanging the polyethylene liner (18). There are no studies comparing methods for debridement, nor can data from the current study be compared directly to data from other studies; however, we postulate that multiple debridements of the infected joint may have an efficacy similar to those of other approaches through a reduction in the microbial burden prior to the commencement of antibiotic regimens with known activity against biofilm-associated bacteria (1, 18–20). Importantly, this study suggests that if mobile parts and liners are not exchanged, a single debridement is not adequate to ensure a reduction in the microbial burden in PJI by MR staphylococci. We postulate that the association of treatment failure and ≥ 4 debridements likely reflects patients with unrecognized treatment failure.

The outcomes reported in previous studies of DAR in this clinical setting are much poorer, with a successful eradication of the infection for only 16 to 37% of patients (2, 7, 17). In many previous studies, patients were managed with 4 to 6 weeks of parenteral vancomycin, and rifampin combination therapy was not routinely administered (2, 7). The addition of rifampin has led to improved patient outcomes for PJI by staphylococci; however, evidence for outcomes of infection with MR staphylococci, particularly MRSA, is conflicting (1, 20). In a previous study by Lora-Tamayo et al., 46% of patients with MRSA infection managed by DAR failed treatment even though the majority of patients received rifampin therapy (18). Rifampin therapy, however, was protective against treatment failure for PJI by methicillin-sensitive and -resistant *Staphylococcus aureus* managed with DAR (18). Similar findings were reported previously by Senneville et al.; however, only 6 cases of PJI by MRSA managed with DAR were included in that cohort (21). Of interest, in the current study, rifampin-resistant *Staphylococcus epidermidis* strains were isolated from 2 patients at initial presentation. These patients were successfully treated with DAR. Current guidelines recommend against debridement and retention if rifampin-resistant staphylococci are isolated from PJI (1). Pristinamycin was administered to 6 patients, including 1 patient with a rifampin-resistant isolate.

The utility of pristinamycin in this clinical setting remains unclear, and further study is warranted.

There have been few studies reporting the outcome of DAR and PJI by coagulase-negative staphylococci. Byren et al. previously reported a success rate of 81% for PJI by coagulase-negative staphylococci managed with DAR, but the proportion of methicillin-resistant isolates was not specified (22). Overall, the current study suggests that outcomes are better for MR-CNS infections managed with DAR, with an overall success rate of 89%.

The duration of antibiotic therapy with DAR has not been well established and is based on expert opinion (1, 23). In this study, patients were treated with a long duration of antibiotic therapy. This differs from other reported recommendations suggesting 3 months for hip PJI and 6 months for knee PJI; however, these recommendations are not specific for the infecting organism (1). There was an association between treatment failure and a duration of antibiotic therapy of less than 90 days; however, this needs to be interpreted with caution, as 8/9 treatment failures occurred early, while patients were still receiving antibiotic therapy, and the duration of therapy was abbreviated because of treatment failure. However, it is an interesting observation that there was no difference observed for patients receiving antibiotic therapy for more than 3 months.

Of the patients receiving rifampin combination therapy, rifampin resistance developed in 3 isolates (7%) and was observed in a newly isolated pathogen from 1 patient. All patients were receiving combination therapy of rifampin and fusidic acid. A similar rate of resistance was reported previously by Lora-Tamayo et al. (18). For two of the patients with a subsequent isolation of a rifampin-resistant strain, there was documentation of poor adherence to medication. This highlights the importance of strict adherence to rifampin-based therapy to minimize the development of rifampin resistance.

There are little data on the activity of fusidic acid against biofilm-dwelling bacteria; Saginur et al. previously demonstrated bactericidal activity against biofilm-producing staphylococcal strains, including MRSA, with combination therapy of rifampin and fusidic acid (24). Whether rifampin combined with fusidic acid is superior to other agents for the treatment of PJI by MR staphylococci is beyond the scope of the current paper; however, our experience with this combination suggests that fusidic acid is a reasonable companion drug for rifampin (10).

While we report improved success rates for the management of PJI by MR staphylococci, MRSA remains a clinical challenge. MRSA predicted poorer outcomes, with 8 of the 9 treatment failures occurring in PJI by MRSA. As highlighted above, the definition of treatment success used in this study was stringent. Importantly, 87.5% of patients with MRSA retained the original prosthesis after treatment and extended follow-up.

The limitations of this study are those inherent to any retrospective study with a potential for variability in the reporting of clinical data. We attempted to minimize bias through *a priori* definitions and data collection by a single researcher. Secondly, the majority of patients in this cohort presented with early PJI; therefore, the results of this study cannot be extrapolated to delayed and late infections.

The particular strength of this study was the homogeneity of the patient population and surgical management according to an established protocol. While larger studies are invaluable to guide

therapy, the heterogeneity of these larger studies often presents significant challenges for data analysis.

Conclusions. This paper describes the outcomes of PJI by MR staphylococci managed by debridement and retention in which the majority of patients received rifampin and fusidic acid combination therapy. The outcomes are comparable with those of the gold standard of treatment, two-stage exchange. Therefore, DAR could be considered for carefully selected patients with PJI by MR staphylococci.

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